Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

Basic Structure of N-(Aryl Substituted) - naphthalidimides

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

NAT2

1X (1-methylxanthine)

$$H_3C$$
 NH_2
 CH_3
 CH_3

AAMU (5-acetamino-6-amino-methyluracil)

AFMU (5-acetamino-6-formylamino-methyluracil)

Fig. 2

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP1A2

$$H_3C$$
 CH_3
 CH_3

Caffeine (1,3,7-trimethylxanthine)

1,7-DMX (1,7-dimethylxanthine)

1,7-DMU (1,7-dimethyluracil)

Fig. 3

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP3A4

MDZ (Midazolam)

1-OH-MDZ (1-Hydroxymidazolam)

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

NAT1

p-ASA (p-aminosalicylic acid)

Acetyl-pASA (acetyl-p-aminosalicylic acid)

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2A6

Coumarin

7-Hydroxycoumarin

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2C19

R-(-)-Mephenytoin

S-(+)-Mephenytoin

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2C9

(s)-Ibuprofen

2-carboxvibuprofen

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2D6

Dextromethorphan

Dextrorphan

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2E1

Clorzoxazone

6-Hydroxychlorzoazone

Title: USE OF METABOLIC PHENOTYPING....

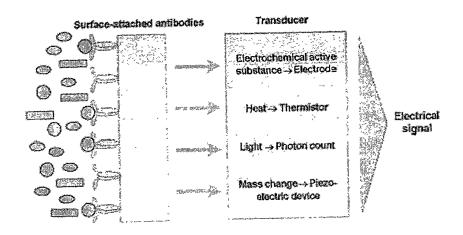


Fig. 11

Title: USE OF METABOLIC PHENOTYPING....

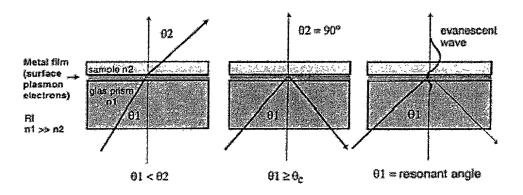


Fig. 12

Title: USE OF METABOLIC PHENOTYPING....

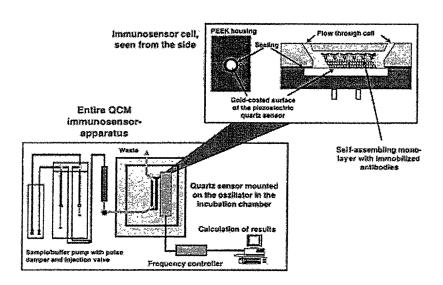


Fig. 13

 NH_2 ÇH₂ HŅ ÇH₂ CH₃O CH₃O МH ΝΉ III I II CH₃ ÇH₂ CH₃ NH ΝΉ ÇH₂ МH CH₃O ИŃ IV CH₃ NH₂ CH₃ ΝΉ NH₂ ΝŃ ИИ VII VI CH₂-CH₂-COOH CH₃ ΝΉ NH₂ COOH . VIII ŃH IX

AAMU-hemisuccinic acid

1 methyl xanthine-8-propionic acid

Fig. 14

Derivatives of AAMU (5-acetamino-6-amino-3-methyluracil) or AFMU (5-acetamino-6-formylamino-3-methyluracil)

X

 (CH_2) n-COOH

where n = 2,3 or 4

$$(CH_2)$$
 $n-C-NH-NH_2$

$$(CH_2) n - C - NH - (CH_2) n - NH_2$$

 $CH_2 - X'$

where X' is I, Br, or C1

$$CH_2-S-(CH_2)n-NH_2$$

$$CH_2 - S - CH_2 - CH_2 - OH$$

Derivatives of AAMU (5-acetamino-6-amino-3-methyluracil) or AFMU (5-acetamino-6-formylamino-3-methyluracil)

Where Y is

H or C-H

Х

$$(CH_2)n-COOH$$

where n = 2,3 or 4

$$(CH_2)n-C-NH-NH_2$$

$$(CH_2)n-C-NH-(CH_2)n-NH_2$$

$$CH_2-X$$

where X' is I, Br, or Cl

$$CH_2-S-(CH_2)n-NH_2$$

$$\mathrm{CH_2}\mathrm{-s-CH_2}\mathrm{-cH_2}\mathrm{-oH}$$

Derivatives of 1X (methylxanthine)

$$\begin{array}{c|c}
O & M & M \\
\hline
O & M & M \\
\hline
O & M & M
\end{array}$$

X

$$(CH_2)n-COOH$$

where n = 2,3 or 4

$$(CH_2) n - C - NH - (CH_2) n - NH_2$$

$$(CH_2) n - C - NH - (CH_2) n - SH$$

Derivatives of 1X (methylxanthine)

 \mathbf{X}

$$(CH_2)$$
 $n-COOH$

where n = 2,3 or 4

$$(CH_2) n - C - NH - (CH_2) n - NH_2$$

$$(CH_2) n - C - NH - (CH_2) n - SH$$

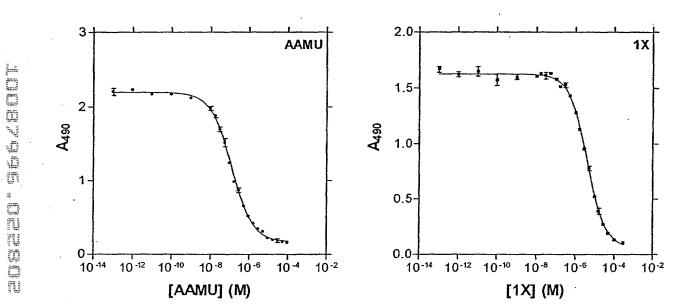
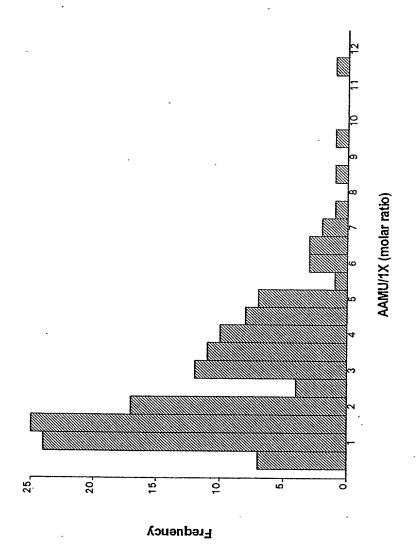


Fig. 19



Docket No.: 3298,1003-000 Title: USE OF METABOLIC PHENOTYPING....

Caffeine derivative

1,7-dimethylxanthine derivative

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Fig. 21

$$\begin{array}{c} O & (CH_2)_4NHBOC \\ CH_3 & N & COOCH_2CH_3 \\ O & N & NH_2 & O & N & N \\ XV & XVI & XVI & XVI \end{array}$$

The first first

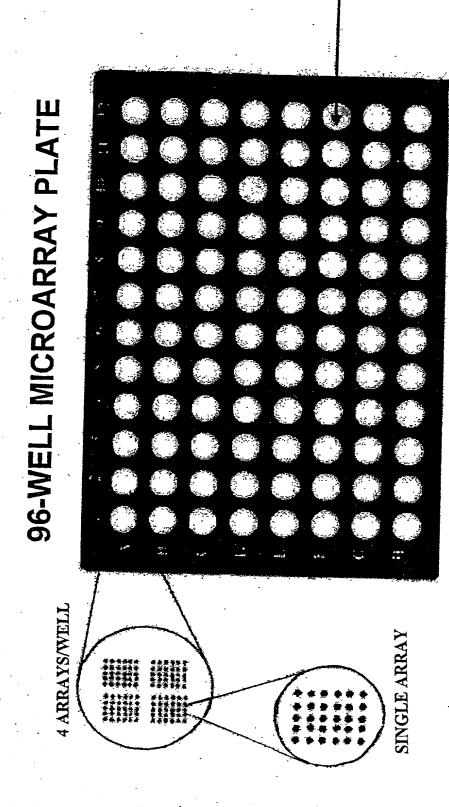
1,7-dimethyluric acid derivative

•									
12	STD16	STD17	STD18	STD19		STD21	STD22	STD23	
다 근	STD8	STD9	STD10	STD11	STD12	STD13	STD14	STD15	
10	Blk	STD1	STD2	STD3	STD4	STD5	STD6	STD7	
σ	85	86	87	88	89	810	S11	S12	
ω	88	810	S11	812	81	\$2	833	24	
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H	Blk	STD1		STD3	STD4	STD5	STD6	STD7	
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Inventor: Brian Leyland-Jones Docket No.: 3298.1003-000

ANTIGEN KEY:	1. BIOTINYLATED BSA MARKER 2-6. BUFFER BLANKS 7. NAT2: AAMU	8. BIOTINYLATED BSA MARKER 9. NAT2: 1X 10. NAT1: DASA	Z O E	13. BIOTINYLATED BSA MARKER 14. CYP1A2: 1,7-DMX 15. CYP1A2: 1,7-DMU		••	19. BIOTINYLATED BSA MARKER 20. CYP2C19: S-(+)-MEPHENYTOIN		22. CYP2C9: 4-HYDROXYDICLOFENAC 23. CYP2D6: DEXTROMETHORPHAN		. BIOTINYLATE	. CYP2E1:	27. CYP2E1: 6-HYDROXYCHLORZOXAZONE	. CYP3A4:	30. BUFFER BLANK	31-36. BIOTINYLATED BSA MARKER
	(g)	(E)	(¥)	(F)		<u> </u>		(;)								
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Docket No.: 3298.1003-000 Title: USE OF METABOLIC PHENOTYPING....



Inventor: Brian Leyland-Jones Docket Mo.: 3298,1003-000

Title: USE OF METABOLIC PHENOTYPING....

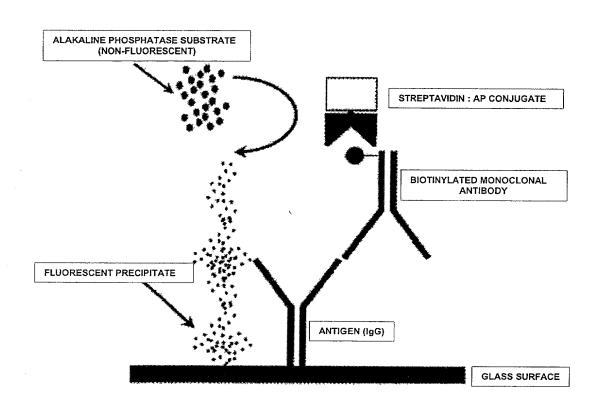


Fig. 26

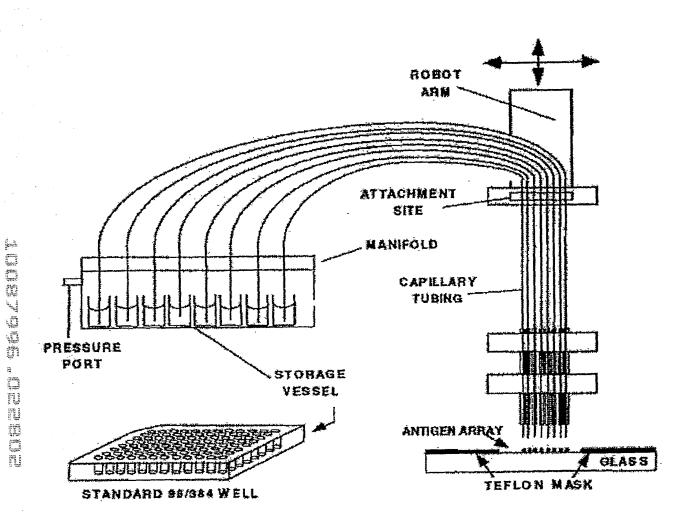
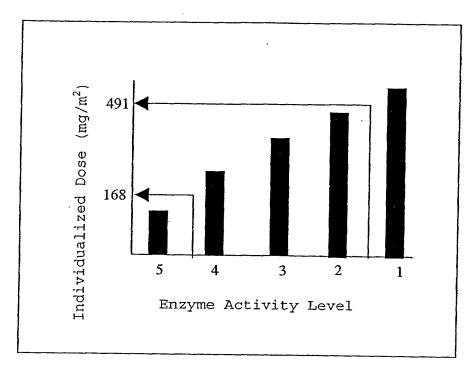


Fig. 27

Title: USE OF METABOLIC PHENOTYPING....



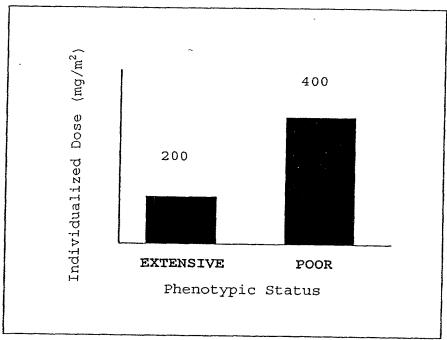


Fig. 28

Docket No.: 3298.1003-000

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

Nomogram for the Determination of Body Surface Area (BSA)

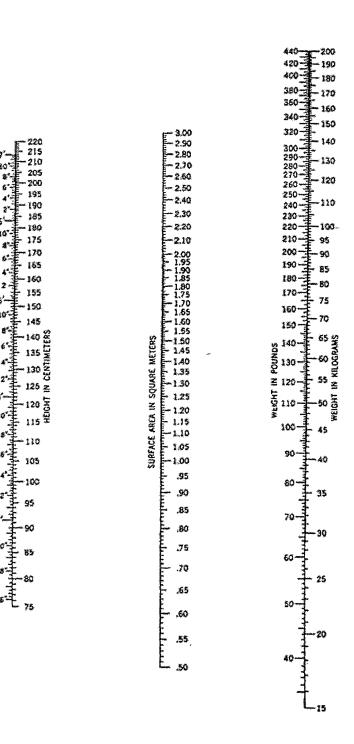


Fig. 29